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Patents ADP number *(if you know it)*
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4. Title of the invention
MULTI-REFLECTING TIME-OF-FLIGHT MASS SPECTROMETER AND A METHOD OF USE

5. Name of your agent *(if you have one)*
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DUPLICATE

MULTI REFLECTING TIME-OF-FLIGHT MASS SPECTROMETER AND A METHOD OF USE

FIELD OF THE INVENTION

The invention generally relates to the area of mass spectroscopic analysis, and more in particularly is concerned with the apparatus, including multi reflecting time-of-flight mass spectrometer (MR TOF MS) and a method of use.

STATE OF THE ART

Mass spectrometry is a well recognized tool of analytical chemistry, used for identification and quantitative analysis of various compounds and their mixtures. Sensitivity and resolution of such analysis is an important concern for practical use. It has been well recognized that resolution of TOF MS scales with flight path. To raise the flight path while keeping moderate physical length there have been suggested multi-reflecting time-of-flight mass spectrometers (MR TOF MS). The use of MR TOF MS became possible after introduction of an electrostatic ion mirror with time-of-flight focusing properties. In reference to US 4,072,862, to a Soviet Patent SU198034 and to Sov. J. Tech. Phys. 41 (1971) 1498, Mamyrin et. al. used an ion mirror for improving a time-of-flight focusing in respect with ion energy. The use of ion mirror automatically causes a single folding of ion flight path.

H. Wollnik realized a potential of ion mirrors for implementing a multi-reflecting MR TOF MS. UK patent GB2080021 suggests an elegant way of reducing full length of the instrument by folding ion path between multiple gridless mirrors. Two rows of such mirrors are either aligned in the same plane or located on two opposite parallel circles (Fig.1). Introduction of gridless ion mirrors with spatial ion focusing reduces ion losses and keeps the ion beam confined regardless of number of reflections (more details in US5017780). Gridless mirrors of GB2080021 also provide 'independence of ion flight time on the ion energy'. Two types of MR TOF MS are disclosed:

(A) 'folded path' scheme, which is equivalent to combining N sequential reflecting TOF MS, and where the flight path is folded along a jig-saw trajectory;

(B) 'coaxial reflecting' scheme, which employs multiple ion reflections between two axially aligned ion mirrors using pulsed ion admission and release.

The 'coaxial reflecting' scheme is also described by H. Wollnik et.al. in Mass Spec. Rev., 1993, 12, p.109 and is implemented in the work published in the Int. J. Mass Spectrom. Ion Proc. 227 (2003) 217. Resolution of 50,000 is achieved after 50 turns in a moderate size (30cm) TOF MS. Gridless and spatially focusing ion mirrors indeed preserve ions of interest (losses are below factor of 2), though the admitted mass range shrinks proportionally with a number of cycles.

Another type, cyclic MR TOF MS is described in papers by H. Wollnik, Nucl.Instr. Meth., A258 (1987) 289, and Sakurai et al, Nucl. Instr. Meth., A427 (1999) 182. Ions are kept in closed orbits using electrostatic or

magnetic deflectors. Usually scheme employs multiple repetitive cycles, which shrinks mass range, similarly to the coaxial reflecting scheme.

SU1725289 by Nazarenko et.al. (1989) introduces an advanced scheme of a folded path MR TOF MS, using two-dimensional gridless mirrors. The MR TOF MS comprises two identical mirrors, built of bars, parallel and symmetric with respect to the median plane between the mirrors and also to the plane of the folded ion path (Fig. 2). Mirror geometry and potentials are arranged to focus ion beam spatially across the plane of the folded ion path and to provide second-order time of flight focusing in respect with ion energy. Ions experience multiple reflections between planar mirrors, while slowly drifting towards the detector in a so-called shift direction (here X axis). Number of cycles and resolution are adjusted by varying an ion injection angle.

The work is considered as a closest prototype of the present invention, since it employs 'folded path' MR TOF MS with planar gridless mirrors, having spatial and time-of-flight focusing properties. However, the MR TOF MS of the prototype provides has no ion focusing in the shift direction, thus, essentially limiting the number of reflection cycles. Besides, similarly to prior art, the ion mirrors used in the prototype do not provide time-of-flight focusing with respect to spatial ion spread across the plane of the folded ion path, so that a use of diverging or wide beams would in fact ruin a time-of-flight resolution and would make an extension of flight path pointless. In other words, the scheme fails delivering wide acceptance of analyzer and thus an ability of working with real ion sources. Finally, the prototype has no implication on the type of ion source, and on efficient ways of coupling between MR TOF MS and various ion sources.

Type of ion source, its spatial and timing characteristics of ion beam, as well as geometrical constrains are the important considerations in the design of MR TOF MS. Compatibility with singly reflecting TOF MS does not automatically mean that a source is well suited for MR TOF MS. For example, pulsed ion sources, like SIMS or MALDI, are well compatible with TOF MS and such instruments are characterized by high resolution and moderate ion losses caused by spatial ion divergence. Switching to MR TOF MS introduces new problems. On one hand, a pulsed nature of such sources suits well an extension of flight time in MR TOF MS, since frequency of ionizing pulses is adjustable. On the other hand, instability of MALDI ions is a limiting factor on flight time extension. A use of MR TOF MS would also reduce solid angle of the detector proportionally to square of the total ion flight path, thus deteriorating sensitivity.

Gaseous ion sources, like ESI, APCI or ICP are known to produce stable ions, but they generate an intrinsically continuous ion beams, or quasi-continuous ion beams, as in case of recently introduced gas filled MALDI ion source (US6331702, US6504150). TOF MS has been successfully coupled with continuous, and later to quasi-continuous ion sources, after introduction of an orthogonal ion acceleration scheme (o-TOF MS) (WO9103071, Soviet patent SU1681340), efficiently converting continuous ion beams into ion pulsed packets. Gaseous ion sources in combination with collisional cooling ion guide (US4963736) produce cold ion beams with low velocity spread along the axis of TOF MS, which help achieving high TOF resolution, in excess of 10,000.

Melvin A. Park in US 6107625 points that further raise of resolution of o-TOF MS is mostly limited by a so-called 'turn-around time' and increasing of flight path improves resolution. He suggests a coupling of external ESI source to a 'coaxial reflecting' MR TOF MS via an orthogonal accelerator, combined with an ion mirror and

multiple deflectors (Fig.3). To improve sampling of continuous ion beam the interface employs a linear ion trap, storing ions between rare ion pulses. In reference to Melvin Park et. al. 'Analytical Figure of Merits of a Multi-Pass Time-of-Flight Mass Spectrometer', extended abstract on ASMS 2001, www.asms.org, the MR TOF MS has demonstrated resolution of 60,000 using 6 cycles of reflections in a c.a. 1m long instrument. However, the use of ion mirrors with grids causes severe ion scattering and ion losses. Coaxial reflecting MR TOF MS improves resolution but shrinks mass range proportionally.

ESI with orthogonal injection has been also coupled to an MR TOF MS with a folded ion path (see EP 1 237 044 A2 and J. Hoyes et al. in extended abstract ASMS 2000 'A high resolution Orthogonal TOF with selectable drift length' www.asms.org). The invention allows converting an existing commercial o-TOF into a dual reflecting instrument by introducing an additional short reflector between orthogonal source and detector. Number of ion reflections is controlled by adjusting energy of continuous ion beam. The 'folded path' MR TOF MS retains full mass range and considerably improves resolution, but it also reduces duty cycle and geometrical efficiency of ion sampling into the orthogonal accelerator.

The two above examples demonstrate that a conventional orthogonal acceleration becomes inefficient in MR TOF MS, particularly at extended flight times. There have been multiple attempts of improving pulsed ion sampling from continuous ion beams, mostly employing ion storing in radio-frequency (RF) traps, like 3-D ion trap (IT), linear ion trap (LIT) in US5763878, US6545268 and WO9930350 or dual LIT (GB2378312). Since all of those solutions compromise temporal and/or spatial spread of ejected ion packets, the orthogonal injection is still the method of choice for singly reflecting TOF MS. Some trapping features are used in an intermediate scheme in US6020586, combining both an ion trapping step and an orthogonal acceleration. Slow ion packets are periodically ejected out of storing ion guide into a synchronized orthogonal accelerator. Compared to conventional o-TOF MS the scheme improves sensitivity, while moderately sacrificing resolution and mass range. The scheme has been coupled to coaxial MR TOF MS in already described reference by M. Park.

Summarizing the above, the MR TOF MS of the prior art do not have spatial and time of-flight focusing providing a certain retaining of ion beam along a substantially extended flight path. Most of references describe MR TOF analyzer without considering their compatibility with ion sources. In fact, a limited acceptance of the known MR TOF analyzers seriously limits such coupling and is expected to cause ion losses at substantially elongated flight paths. Some references are made to actual coupling of MR TOF MS to continuous ion sources, demonstrating strong improvement of resolution. However, resolution is gained at the expense of losing sensitivity and, in the case of coaxial reflections, of shrinking mass range. Therefore, there is a need for TOF mass spectrometer working with intrinsically continuous or quasi-continuous ion sources, and superior to o-TOF by a set of major analytical characteristics, namely – sensitivity, mass range and resolution.

SUMMARY OF THE INVENTION

The inventors have realized that acceptance and resolution of MR TOF MS with two-dimensional planar mirrors could be substantially increased by:

(A) using a periodic set of lenses in a drift space, providing focusing in a shift direction;

(B) employing a geometry of planar mirrors with at least 4 electrodes, which allows not only a known spatial ion focusing and a time-of-flight focusing with regards to energy, but also a novel time-of-flight focusing with regards to spatial spread.

The inventors further realized that an improved acceptance of the MR TOF MS of the invention allows its efficient coupling to continuous ion sources via an ion storing device. Continuously arriving ions could be stored and pulse ejected out of a storing device, such as ion guide, IT, LIT, thus saving ions between rare pulses of MR TOF MS, sparse compared to o-TOF MS.

The MR TOF MS of the invention provides an advantageous combination of ion optics features, compared to prior art, since:

- It has a full mass range, a property of a 'folded path' scheme;
- It eliminates ion losses on meshes, since mirrors are gridless,
- It efficiently consumes continuous ion beams by storing ions in an ion trap with pulse ion ejection at lower frequency;
- It accepts wide ion beam out of such traps, since the analyzer has a spatial focusing by periodic lens in a shift direction and spatial focusing by mirrors across the plane of the folded ion path;
- It improves resolution by providing a high-order time-of-flight focusing with respect to energy and, which is novel, to spatial spread of ion packets;
- It tolerates a larger turn-around time of ion packets by extension of the flight time, using folded path in multiple reflections of a well confined ion beam;
- The longer flight time brings a by-product advantage – slower and less expensive detector and data acquisition system, both currently being costly parts.

The invention introduces a completely novel to MR TOF MS feature - multiple lenses, optimally positioned in the middle of drift space with a period corresponding to ion shift per integer number of turns. Periodic lenses allow focusing of the beam and, thus, insure a stable confinement of ions along an extended folded ion path. The set of lenses brings the novel quality to MR TOF: beam spatial and angular spreads stay limited even after an extremely large number of reflections (actually achieved if using reflections in the shift direction). Even more, using ion optics simulation the inventors found out that ion motion in the novel MR TOF efficiently withstands various external distortions, like inaccuracy of geometry, stray electric and magnetic fields of pumps and gauges, as well as space charge of the ion beam itself. The MR TOF returns ions into vicinity of main trajectory in spite of those distortions, similar to trapping in the potential grove. The feature of periodic lenses allows compact packaging of MR TOF MS with an extended flight path, combined with a confident full transmission of ion beam.

The lens tuning allows periodic, repeatable focusing in a shift direction, achieved when focal length F matches an integer number of half reflections or quarters of full ion turns (P/4), F=N*P/4. The most tight focusing occurs when F=P/4. Such tight focusing is advantageous for minimizing shift per turn and making instrument compact. It is important that even under the condition of such tight focusing lenses remain weak because of a relatively long ion path per turn, and therefore they introduce only minor incorrigible time-of-flight aberrations with respect to the ion spatial spread in the plane of the folded ion path. Planar lenses, substantially elongated across the plain of ion path, provide an advantage of fairly independent tuning of spatial focusing by ion mirrors and by

periodic lenses, since they focus in different directions. Besides, such lenses may also incorporate steering by using asymmetric voltages on side plates.

The invention allows further increase of the flight path length by employing reflections in a shift direction. Such reflections can be achieved, for example, by deflection plates, located on the sides of shift path in the middle of drift space between the mirrors. Deflection plates could operate constantly or in a pulsed mode to allow ion gating. A single reflection does not affect mass range, while a further raise of the flight path by additional reflections is achieved at the expense of mass range. The deflection plates could be also used to bypass the analyzer and to steer ions into a receiver.

Novel focusing properties of the mirrors of the invention are provided by choosing a proper distance between the mirrors and adjustment of electrode potentials. Such adjustment results in the 3rd-order time-of-flight focusing in ion energy, 2nd-order time-of-flight focusing with respect to the spatial ion spread across the plane of the folded ion path and spatial focusing across the said plane. The inventors realized that elimination of high-order time-of-flight aberrations is stable with respect to assembly defects as well as to moderate variations of the drift lengths and electrode potentials. Therefore, a high resolving power could be obtained by tuning of novel MR TOF MS while adjusting only one electrode potential, in fact, varying one parameter – a linear dependence of the ion flight time on the ion energy.

The just described focusing properties are realized, for example, in planar 4-electrode mirrors, composed of thick square frames, substantially elongated in a shift direction. The desired field structure also could be made using thin plates with slots, bars, cylinders, or curved electrodes. The edges of two-dimensional mirrors could be efficiently terminated using printed circuit boards to shorten the total physical length of the MR TOF MS. Having more electrodes is very likely to further improve mirror parameters, but complicates the system.

In a preferred mode the ion source and the ion detector are located in the drift space between the mirrors. In such configuration the folded ion path remains far from mirror edges and the mirrors can be operated in a constant mode to achieve better stability and mass accuracy of the MR TOF MS. However, the invention is well compatible with a pulsed ion admission from external source or ion release through ion mirrors in order to couple the MR TOF MS with external ion sources or ion receivers and to avoid beam passage through fringing fields of mirror edges.

The invention is applicable to various ion sources, including pulsed ion sources, like MALDI or SIMS, quasi- continuous ion sources, like MALDI with collisional cooling, as well as intrinsically continuous ion sources like ESI, EI, CI, PI, ICP or a fragmenting cell of a tandem mass spectrometer. All continuous or quasi-continuous ion sources preferably operating with an ion guide.

As mentioned earlier, having a much wider acceptance, the MR TOF MS of the invention can be used in conjunction with an ion storing device, avoiding ion losses between rare accelerating pulses. Such ion storing can occur in gas filled radio frequency (RF) storing devices of various kinds, including ion guides, RF channels, IT or LIT, incorporated either into an ion source itself or into an accelerator of the MR TOF MS. The invention employs either

a direct acceleration out of an ion storing device, axial or orthogonal,

or a dual acceleration scheme, where slow ion pulse is ejected out of the storing device with consecutive pulsed acceleration, axial or orthogonal,

or a dual storage scheme, where slow ion pulses are admitted into the second trap usually operated at a lower gas pressure. Ion ejection out of the second storing device can be also made axially or orthogonally, or via an additional accelerator, axial or an orthogonal.

Some compromises in parameters of ion packets are acceptable because of substantial extension of flight path and wide acceptance of the novel MR TOF MS.

The preferred embodiment of the invention employs the latter- more complex, but advantageous scheme of dual ion storage. Ion guides are preferred choice for both storage devices. It is preferable using an additional set of pulsed electrodes, whose field well penetrates into ion storage area of the second ion guide and allows fast ion ejection in axial direction with a small turn around time, while providing fairly uniform accelerating field and a moderate ion divergence. Compared to orthogonal acceleration scheme the invention provides an almost complete utilization of continuous ion beam. Some increase of the turn around time is compensated by an extension of the flight path.

The scheme is expected to provide a complete utilization of continuous or quasi-continuous ion beam as well as an improved resolution, in the range of R~100,000. The MR TOF MS could be used either as a stand-alone instrument, or as a part of LC-MS or MS-MS tandem, mostly expected as a second analyzer of fragment ions, combined with any know mass separator of parent ions and a with any known kind of fragmenting cell.

The MR TOF MS of the invention could be used as a first, separating mass spectrometer in a tandem mass spectrometer arrangement. The advantage of using MR TOF becomes apparent in a co-pending patent by one of the authors. The co-pending invention suggests using slow TOF1 for ion separation, combined with a fast TOF2 for fragment analysis. The arrangement allows parallel analysis of multiple precursors per single pulse out of ion source. Current invention allows particularly long separation in MR TOF MS, as well as separation at low and medium energy of ion beam, tight focusing of the beam and precise control of ion beam location, useful while directing the beam into a fragmenting cell.

BRIEF DESCRIPTION OF THE DRAWINGS

For a more complete understanding of the present invention, reference is now made to the following drawings in which:

Fig.1 show a multi-reflecting time-of-flight mass spectrometer (MR TOF MS) of prior art, by Wollnik et.al., GB patent No 2080021 (fig.3 and fig.4 of the GB patent).

Fig.2 shows a 'folded path' MR TOF MS of a prototype by Nazarenko et.al., SU1725289.

Fig.3. shows a 'coaxial reflecting' MR TOF MS of prior art by M. Park, US 6107625.

Fig.4. shows a schematic of the preferred embodiment of the MR TOF MS of the invention, with details on novel periodic lenses.

Fig.5 shows MR TOF analyzer of the preferred embodiment of the invention, describing geometry and potentials of ion mirrors, providing a novel type of spatial and time-of-flight focusing.

(OR: Fig. 5 shows geometry and potentials of ion mirrors of the preferred embodiment of the invention)

Fig.6 shows a schematic and principles of ion path extension by ion reflections in the shift direction within the MR TOF analyzer of the preferred embodiment of the invention.

Fig.7 shows a generalized schematic of ion sampling from continuous ion sources into the MR TOF MS of the invention using an intermediate ion storage device, wherein:

Fig 7A shows a block diagram of the entire MR TOF MS;

Fig. 7B shows details of the ion source and of the ion guide;

Fig. 7C shows details of the second storage device and of the ion accelerator.

Fig. 8 shows the detailed schematics of the preferred embodiment of MR TOF MS of the invention.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The present invention relates generally to the area of mass-spectroscopic analysis, and more in particular is concerned with the apparatus, including a multi reflecting time-of-flight mass spectrometer (MR TOF MS). More specifically, the invention improves resolution and sensitivity of planar and gridless MR TOF MS by employing a novel arrangement and control of mirror electrodes in combination with a periodic set of lenses in a drift space. Because of improved spatial and time focusing, the MR TOF MS of the invention has a wider acceptance and confident confinement of ion beam along an extended folded ion path. As a result, the MR TOF MS of the invention can be efficiently coupled to continuous ion sources via an ion storing device, thus saving on duty cycle of ion sampling.

Fig.1 shows a multi-reflecting time-of-flight mass spectrometer (MR TOF MS) of prior art, by Wollnik et.al., GB patent No 2080021 (fig.3 and fig.4 of the GB patent). In a time-of-flight mass spectrometer ions of different masses and energies are emitted by a source 12. The flight path of ions to a collector 20 is folded by arranging for multiple reflections of the ions by mirrors R1, R2, ... Rn. The mirrors are such that the ion flight time is independent of ion energy. Preferably ions of different energies are allowed to bunch. The patent shows two geometrical arrangements of multiple axially symmetric ion mirrors. In both arrangements ion mirrors are located in two parallel planes I and II and are aligned along the surface of ion path. In one arrangement this surface is a plane and in another one it is a cylinder. Note that ions travel at an angle to optical axis of ion mirrors which induces additional time-of-flight aberrations and thus considerably complicates achieving high resolution.

Fig.2 shows a 'folded path' MR TOF MS of a prototype by Nazarenko et.al., described in Russian patent SU1725289. The MR TOF MS of the patent comprises two gridless electrostatic mirrors, each composed of three electrodes 3, 4 and 5 for one mirror, and 6, 7 and 8 for another mirror. Each electrode is made of a pair of parallel plates 'a' and 'b', symmetric with respect to the 'central' plane XZ. A source 1 and receiver 2 are located in the drift space between the said ion mirrors. The mirrors provide multiple ion reflections. Number of reflections is adjusted by moving the ion source along the X axis relative to the detector. The patent describes a type of ion focusing which is achieved on every ion turn, achieving a spatial ion focusing in Y direction and a second order time of flight focusing with respect to ion energy.

Note that the prototype provides no ion focusing in the shift direction, thus, essentially limiting the number of reflection cycles. It also does not provide time-of-flight focusing with respect to spatial ion spread in Y direction. Therefore, the MR TOF MS of the prototype fails delivering wide acceptance of analyzer and thus an ability of

working with real ion sources. Finally, the prototype has no implication on the type of ion source, and on efficient ways of coupling of MR TOF MS to various ion sources.

Fig.3. shows a 'coaxial reflecting' MR TOF MS of prior art by A. Park, US 6107625.The invention comprises two electrostatic reflectors 34 and 38, positioned coaxially with respect to one another such that ions generated by an ion source 32 can be reflected back and forth between reflectors. The first reflecting device 34 combines functions of an orthogonal accelerator and of an ion mirror. After multiple ion reflections either of mirrors is rapidly switched off to allow the ions to pass through the reflector and onto an ion detector 36. The patent teaches a way of coupling of continuous ion source to an MR TOF MS. The described apparatus indeed achieves high resolution within a small size instrument. However, an employed 'coaxial reflecting' scheme strongly reduces mass range and decreases the duty cycle of ion sampling from a continuous ion beam. Meshes cause substantial ion losses. Duty cycle is improved in a later work by author after introducing an LIT into the interface.

Fig.4. Fig.4. shows a schematic of the preferred embodiment of the MR TOF MS of the invention, with details on novel periodic lenses. The MR TOF MS 11 comprises a pulsed ion source 12 with a built in accelerator 13, an ion receiver 16, a set of two gridless ion mirrors 15, parallel to each other and substantially elongated in a 'shift' direction, denoted here as Y axis, a field-free space 14 between the said mirrors and a set of multiple lenses 17, positioned in the said drift space.

The above elements are arranged to provide a folded ion path 19 between the ion source 12 and the ion receiver 16, the said ion path being combined of multiple reflections between the ion mirrors 15 and of an ion drift in the shift Y direction. The shift is arranged by slight tilting, mechanically or electronically, of the incoming ion packets in respect with the X axis. The lenses 17 are positioned along the Y axis with a period corresponding to ion shift per integer number of ion reflections. The preferred embodiment strongly enhances acceptance of the MR TOF MS by providing novel ion optics properties - periodic focusing by lenses 17 in the shift Y direction, complementing a periodic spatial focusing in the orthogonal Z direction, provided by planar gridless ion mirrors. Those ion optics properties as well as improved time-of-flight focusing by specially designed ion mirrors of the invention are discussed below in more details.

Incorporation of periodic lenses is a completely novel feature in MR TOF MS, which provides a stable retaining of the ions along the main jig-saw folded ion path. The lens tuning allows periodic, repeatable focusing in a shift direction, achieved when focal length F matches an integer number of half reflections or quarters of full ion turns (P/4), F=N*P/4. The most tight focusing occurs when F=P/4. Such tight focusing is advantageous for minimizing shift per turn and making instrument compact. It is important that even under the condition of such tight focusing lenses remain weak because of a relatively long ion path per turn, and therefore they introduce only minor incorrigible time-of-flight aberrations with respect to the ion spatial spread in the plane of the folded ion path. Planar lenses, substantially elongated across the plain of ion path, provide an advantage of fairly independent tuning of spatial focusing by ion mirrors and lenses across the plane of the folded ion path and in this plane, respectively. Besides, such lenses may also incorporate steering by using asymmetric voltages on side plates.

The set of periodic lenses brings the novel quality to MR TOF: beam parameters stay limited even after an extremely large number of reflections (actually achieved if using reflections in the shift direction). Even more, using

ion optics simulation the inventors found out that ion motion in the novel MR TOF efficiently withstands external distortions, like inaccuracies of geometry, stray electric and magnetic fields of surfaces, pumps and gauges, as well as space charge of the ion beam. The MR TOF returns ions into vicinity of main trajectory in spite of those distortions, equivalent to trapping in the potential grove. The feature of periodic lenses allows compact packaging of MR TOF MS with an extended flight path, combined with confident full transmission of ion beam.

Fig. 4 also shows a side view **21** of the same preferred embodiment as well as an axial potential distribution **22** in the analyzer of the preferred MR TOF MS. The mirrors 15 are symmetric with respect to the XY plane and preferably, though not necessarily, identical with respect to each other, i.e. are symmetric around the YZ plane. The mirrors 15 are composed of at least 4 electrodes, comprising a lens electrode 15L, two electrodes 15E and a cap electrode 15C in addition to a specially formed edge of the drift space 14D. As mentioned, the mirrors are substantially elongated in a shift direction, forming a two-dimensional electrostatic field around the area of the folded ion path 19.

Novel focusing properties of the mirrors of the invention are provided by choosing a proper distance between the mirrors and adjustment of electrode potentials. The inventors have found such parameters by ion optics simulations with a built in calculation of derivatives and also with a built in automatic optimization block. Working with such home made program the inventors have formulated some general trends of optimization algorithm and several key requirements to the ion optics of ion mirrors. For example, for symmetric MR TOF MS with two identical mirrors, each mirror should comprise at least 4 electrodes in order to have 5 independently tuned parameters:

a) 3 parameters (optimally two electrode potentials and the drift length between the mirrors) are chosen to provide a periodic (after each reflection) third-order time-of-flight focusing with respect to energy, i.e. the tuning allows eliminating the first, second and third-order derivatives of the ion flight time on the ion energy;

b) one parameter (optimally the potential of the 'incorporated lens' electrode closest to the drift space) provides a so-called 'parallel-to-point' spatial focusing across the plane of the folded ion path. Such term means that a parallel ion packet, starting in the middle of drift space, will be focused into a point after half a turn and will be converted back into a parallel ion packet after a full turn. Advantageously this focusing is arranged so that ions of the packet also intersect a plane of ion path in the vicinity of turning point;

c) one remaining parameter is adjusted to eliminate the second-order derivative of the flight time of the just mentioned ion packet with respect to the initial ion offset from the plane of the folded ion path.

If both conditions (b) and (c) are satisfied, then the symmetry of the mirror arrangement automatically leads to elimination of all time-of-flight aberrations up to the second order on the initial coordinate and angular spread across the plane of the folded ion path after each full turn, which is after an even number of reflections.

The inventors realized that elimination of high-order time-of-flight aberrations is stable with respect to assembly defects as well as to moderate variations of the drift lengths and electrode potentials. Therefore, a high resolving power could be obtained by tuning of novel MR TOF MS while adjusting only one electrode potential, in fact, varying one parameter – a linear dependence of the ion flight time on the ion energy.

Fig.5 shows particular examples of geometry and voltages of MR TOF analyzer of the invention, which provide a just described high order spatial and time-of-flight focusing. The view **23** shows dimensions of the particular 4 electrode mirror with sizes being normalized to a length L of typical electrode. As before, the electrodes of the mirror are denoted as 15L for lens electrode, 15E for two middle electrodes and 15C for a cap electrode. Similarly, the view **24** shows dimensions of the drift space and of the entire mirror, while the view **25** shows potentials on electrodes of the same particular MR TOF MS. The potentials are normalized to the nominal energy E of the ion beam. The analyzer forms an axial potential distribution similar to one shown on the view **22** of **Fig. 4.**

The elongated two-dimensional structure of ion mirror could be formed using electrodes of various shapes. The view **26** of **Fig.5** shows few possible types of electrode geometry, including elongated square frames, thin plates with elongated slots, square bars and not shown types formed by parallel rods, curved electrodes, like cones, hyperbolas, etc. The inventors also expect that a desired structure of electric field could be synthesized using fewer number of two-dimensionally shaped electrodes.

To preserve a two-dimensional field structure requires a special treatment of a boundary problem. To avoid distortions of the field structure the mirrors are either made much longer than the total shift of the folded ion path, or employ special devices, like for example a fine-structured printed circuit boards (PCB) 30 with a shape of electrodes repeating a shape of equipotential lines of the mirror field. In our ion optics simulations we found that a simple adjustment of width of the lens edge allows noticeable reduction of fringing field penetration. Similar results could be obtained by introducing an additional edge electrode, for example as a rib of the lens electrode 15L.

Fig. 6 shows a schematic and principles of ion path extension by ion reflections in the shift direction within the MR TOF analyzer of the preferred embodiment of the invention. In addition to standard components, which are shown using the same old numbers, the embodiment 31 comprises steering devices 32 and 33 and an optional in-line ion receiver 34. The incident ion packet 35 can be either deflected onto an additional detector 34 or steered into the MR TOF MS along the folded path 36. On the other end of the shift axis Y the second steering device 35 can either release ions onto the ion receiver 16 or steer the ion packet again into the MR TOF MS along the folded ion path 37.

In operation, in a particular regime, when the entrance steering 32 is disabled and the exit steering 33 is constantly on, the MR TOF MS retains a non-repeating folded ion path and thus retains full mass range of mass spectrometric analysis, while doubling the flight path. The entrance steering can be used to by-pass analyzer all along. Such feature appears useful in a co-pending patent, where the MR TOF MS is used as an ion separator of a tandem MS and the bypass feature would allow toggling between tandem and MS-only regimes.

The steering could be used to pass ion packets along a repetitive, cyclic folded ion path, wherein a raise of flight path is accompanied by a proportional shrinking of mass range, a compromise to be made upon requirements of a particular application.

Geometrical constrains of the entire analyzer and a fringing field of mirror edges may become important while using reflections in the drift direction. An optional way around the problem is in passing the ion beam through ion mirrors, more specifically, through the slit in the mirror cap electrode 15C. The mirror 15 then can be extended, e.g. as shown by dashed line, and should be turned on and off in a pulsed mode.

A particular example 41 of steering device is shown also on the Fig. 6. The steering device 41 comprises a set of parallel plates 42 to 46, where plates 42 are grounded. The device combines feature of planar deflecting plates and of a planar lens. The device could be either toggled between two functions or could combine two functions simultaneously by tuning voltages on plates 44 and 45. The device allows incorporation into a periodic structure of lenses. In this case, each individual cell could be used for both ion focusing and/or reflection in a drift direction. Deflection plates could operate constantly or in a pulsed mode to allow ion gating, selecting narrow mass range, analyzing multiple precursors or multiple mass windows simultaneously. Flexible switching between lenses and deflectors is also useful while overcoming the problem of fringing fields, since the deflectors can create a closed loop well within boundaries of the unaffected mirror field (not shown).

Introduction of ion deflection causes compromises in time-of-flight resolution, hence they are generally used for ion manipulation, extension of flight time, rather than for improving resolution of the MR TOF MS.

For example, with a typical energy spread of 5 % and the phase space of the beam of 10π mm mrad in both directions normal to the beam path, an ion optical simulation of the MR TOF MS of the invention with L = 25 mm predicts the achievable mass resolving power (FWHM) of 100,000 without using deflectors in the mode with the maximal focal length of the lenses, equal to the length of the full beam turn (two reflections). With the most tight focusing induced by lenses and additional use of deflectors, this resolving power drops down to 30,000. Note however that because of the extended flight time this value can be achieved for a much more loose values of the ion turn around time as compared to the conventional TOF MS with the same resolving power.

Now that we have completed a description of the MR TOF MS of the invention it is of particular importance to note, that the novel MR TOF analyzer has a much higher tolerance to spatial and temporal spreads of ion beam. The novel analyzer provides a stable ion beam confinement, which allows an extension of flight time without causing geometrical ion losses. An extended flight time, in turn, enhances TOF resolution and reduces the effect of ion turn around time, appearing in the pulsed ion source. Finally, the MR TOF MS of the invention also provides a high order time-of-flight focusing with respect to the spatial spread of initial ion beam, i.e. much wider beams can be accepted without loosing time-of-flight resolution. On the other hand an extension of flight time reduces efficiency of ion sampling out of continuous ion beams. The contradiction is resolved with the introduction of another key feature of the invention - incorporation of ion storing and pulse ejection into a continuous or quasi-continuous ion sources.

The invention strongly improves efficiency of ion sampling into an MR TOF MS of the invention by adding an ion storing step for accumulation of continuous ion beam and pulsed ion ejection at a reduced frequency, corresponding to an extended flight time of MR TOF MS. Such ion storing occurs in gas filled radio frequency (RF) storing devices of various kinds, including ion guides, RF channels, IT or LIT, incorporated either into an ion source itself or into an accelerator of the MR TOF MS. The storing step avoids ion losses between rare pulses of any MR TOF MS, such combination has not been described in the prior art.

Fig.7 shows a generalized schematic of ion sampling from continuous ion sources into the MR TOF MS of the invention using an intermediate ion storage device, wherein:

Fig 7A shows a block diagram of the entire MR TOF MS;

Fig. 7B shows details of the ion source and of the ion guide;

Fig. 7C shows details of the second storage device and of the ion accelerator.

In reference to **Fig 7A**, and using a block diagram level of detailing, the entire MR TOF MS of the preferred embodiment of the invention **51** comprises a continuous ion source 61 an ion guide 71 a second storage device 81 an accelerator 91 and an MR TOF analyzer 31, being sequentially interconnected. The block diagram shows the most general case, wherein elements 71, 81 and 91 are optional, i.e. could be either omitted or merged together within some particular embodiments.

In operation, the continuous ion source 61, preferably gaseous ion source, generates a continuous or quasi-continuous ion beam, which is preferably transported within an ion guide 71. Preferably, the ion guide 71 stores continuous ion beam and eject ion packets periodically with a period corresponding to one in the MR TOF analyzer 31. Such ejected ion packets are passed into the accelerator 91, either directly or via an optional, second storage device 81. The accelerator, continuous or pulsed, inject fast ion packets into the MR TOF analyzer, axially or orthogonal. Both, the ion guide 71and the second storage device 81 could be any RF confining and gas filled device of the following list: quadrupole or multipole ion guide, RF channel or a linear ion trap.

The **Fig. 7B** shows particular examples of gaseous ion sources and of the ion guide. The particular example **61A** of continuous, ESI ion source comprises a spraying probe 62, a sampling nozzle 63, a sampling skimmer 64 and a pump 65. The particular example **61B** of a quasi-continuous MALDI ion source with gas cooling comprises a sample plate 67, a laser 68 and a supply 69 of cooling gas. Both ion sources are connected to an ion guide 71. The particular example 71 of the storing ion guide comprises quadrupole rods 72, supplied with radio frequency (RF) voltage, a set of supplementary electrodes 73, an exit aperture 74 and a pump 75.

Components and principles of operation of both ion sources are well described in the art. In the particular example 61A of the shown ESI ion source, a solution of analyte compound is sprayed from the probe 62 in the region with atmospheric pressure. Highly charged aerosol evaporates, thus forming gaseous ions of analyte, which are sampled via the sampling nozzle 63. An excessive gas is evacuated by the pump 65 to a gas pressure of few mbar. Ions are further sampled via the sampling skimmer 64 with assistance of gas flow and electrostatic fields, generating a continuous ion beam 66.

The MALDI ion source 61B with gas cooling generates ions of analyte, while illuminating a sample on a sample plate 67 by the pulsed laser 68. A supply 69 provides a cooling gas around the sample plate at an intermediate gas pressure, around 1mbar. Ions, emitted from the sample plate are cooled and stabilized in gas collisions. Ions stability is particularly important for the use in MR TOF MS, since it employs a prolonged analysis time. Ions kinetic energy and sharp timing characteristics become dampened in gas collisions. The resulting ion beam 66 is considered more as a quasi-continuous ion beam, rather than a pulsed ion beam.

In the present invention, either continuous or quasi-continuous ion beam 66 is directed into the ion guide 71. Ions are sampled via an aperture 64, while an excessive gas is evacuated by the pump 75. The aperture 64 and the pump 75 are similar in cases of both ion sources, because of about equal gas pressure in front of the aperture 64.

Ions are accumulated between RF rods 72, while being dampened in gas collisions and being retarded by apertures 64 and 74. Ions are confined near the axis of RF quadrupole and in the bottom of DC potential well. Periodically ion packets 76 are pulse ejected out of the storing ion guide and into the accelerator 91, either directly or via an optional, second ion storage device 81.

The invention employs an unusual arrangement of ion storing, where axial DC distribution in the ion guide 71 is organized by supplementary electrodes 73. The rods 73 surround the RF rods 72, such that their electrostatic field efficiently penetrates between the rods. The axial DC distribution is adjusted and varied in time to provide a space distributed ion storage, a controlled percentage of ion sampling and a moderate duration of ion ejection process. Note, that manipulations by voltages on the supplementary electrodes 73 do not require any manipulation by RF potentials on RF rods 72. In fact, it is advantageous keeping RF voltage applied to the rods 72 in a steady state, thus, providing a better focused pulsed ion packets. Since ions are ejected along the axis, where the RF field is negligible, the RF field has very little affect on axial ion velocity.

The storing ion guide 71 can be coupled directly to the accelerator 91, preferably orthogonal. Since the ion guide is filled with gas it is preferable using a soft ion ejection by small modulation of potentials on electrodes 73 and 74. Such slow (fewto few tens of electron Volts) and fairly long (several microseconds) ion packets are well compatible with synchronized orthogonal acceleration. The scheme is not shown since it is fairly common in the prior art (e.g. US6020586). The packet 76 passes via an additional differential pumping stage to accommodate the gas filled ion guide to the analyzer at deep vacuum. The additional stage comprises a lens, forming a nearly parallel ion beam. The ion packet enters an orthogonal accelerator 91, synchronously injecting ions into the analyzer. The orthogonal accelerator either being positioned in the drift space of the MR TOF analyzer of the invention, or being combined and pulsed with one of the mirrors of the planar MR TOF analyzer of the invention, or being a pulsed extension of the DC field of one the ion mirror of the invention. Similarly to the prior art, the storage ion guide provides an advantage of saving duty cycle of the orthogonal acceleration at the expense of ion mass range.

Fig. 7C shows details of the second storage device 81. The second storage device 81 comprises a generic ion trap, an exit aperture, either axial 88 or orthogonal 86 and a pump 85. The storage device 81 is connected the ion guide 71, preferably a storage ion guide. There are two schemes shown on the fig 7C. The left scheme corresponds to a direct ion ejection out of the storage device 82 into the MR TOF analyzer, either axially 87 or orthogonal 89. The right scheme corresponds to ion injection via an optional accelerator 91, either axial 94 or orthogonal 93.

The major function of an additional storing device 81 is to prepare an ion cloud at different conditions compared to the rest of ions, stored in the first storing ion guide 71. Such conditions may differ by gas pressure, space charge of ion beam or configuration of ejecting electrodes. As will be shown in the following description, the dual storage scheme is more flexible, allows full utilization of ion beam and a number of automatic adjustments. Most important, it generates ion beam with a smaller phase space and improves beam acceptance by analyzer. The advantages of using an additional storage device will become apparent in the following detailed description of the preferred embodiment of the MR TOF MS of the invention, which employs the dual storage scheme.

Fig. 8 Fig. 8 shows the detailed schematics of the preferred embodiment of MR TOF MS of the invention. The preferred embodiment **101** of the invention comprises sequentially connected main components, comprising a continuous ion source 61, a storing ion guide 71, a second storing ion guide 81, an accelerator 91 and the MR TOF analyzer 31. Each main component comprises earlier described elements. The particular shown example of continuous ion source 61 is an ESI ion source, comprising a spray probe 62, a sampling nozzle 63, a sampling skimmer 64 and a pump 65. The storing ion guide 71 comprises a set of quadrupole RF rods 72, surrounded by supplementary pulsed electrodes 73, an exit aperture 74 and a pump 75. The second storing ion guide 81 comprises a gas confining cap 74C, a set 83 of quadrupole RF rods, surrounded by a set 84 of supplementary pulsed electrodes, an exit aperture 88, a pump 85. The accelerator 91 comprises a set of electrodes 92, a housing 96, shared with the MR TOF MS analyzer and a pump 95. The MR TOF analyzer 31 comprises two planar and gridless ion mirrors 15, an in-line ion detector 16, a set of periodic lenses 17, a set 32 of entrance steering plates, and a set 33 of exit steering plates.

In operation, the ESI ion source 61 generates the continuous ion beam 66, which is stored in the storing ion guide 71 at an intermediate gas pressure (from .01 to .1mbar). The storing ion guide 71 periodically ejects slow ion packets into the second storing ion guide 81, which operates at a lower gas pressure (from 1E-4 to 1E-3 mbar). A gas confining cap 74C allows having a higher gas pressure in the upstream area of the second ion guide 81, thus improving ion dampening and ion trapping in the second ion guide 81. A smaller gas pressure in the second guide 81 helps reducing gas load onto a pump 95 and, thus, helps keeping low gas pressure in the chamber 96 of MR TOF analyzer 31 and accelerator 91, in fact, requiring a lower gas pressure (below 10^{-7} mbar) because of the extended flight path, compared to conventional TOF MS.

The slow ion packet contains a fixed portion of all ions accumulated in the first ion guide 71. As a guiding example, approximately 1% of stored ions are sampled through the aperture 74 in about every 1 ms. Such balance between coming and leaving ions allows refreshing of the ion content in every 100ms. The amount of ions, stored in the first ion guide 71, depends on intensity of ESI in beam. At a typical ion flow of 10^8 ions a second the first ion guide 71 would contain about 10^7 ions, known to build up a noticeable space charge field. This, in fact, is another reason for dual storage arrangement. With only 1% of ions being sampled into the second storage the amount of ions in the second storage is about 10^5. Such ion cloud, being stored in 1mm volume would create about 10meV potential of space charge, being close to thermal energy (gas kinetic energy of 25meV) and moderately affecting ion initial parameters.

The first ion guide 71 ejects slow ion packet by a very gentle pulsed axial field, generated with assistance of pulse potentials on the exit aperture 74 and optionally on the additional electrodes 73. The use of the set 73 of additional electrodes allows an accurate control of energy and amount of ejected ions within the packet. The ejected ion packet is 100% trapped in the second storing ion guide 81, using a pulsed trapping scheme. In more details, a potential on exit aperture 88 forms a repelling DC barrier, while RF field of electrodes 83 confines ions in radial direction. Ion packet gets reflected from the far end (88), however, by the time ions will return to the entrance (74) of the second guide 81, they will see a repelling potential of electrode 74, which was raised after completion of ion ejection from the first ion guide 71. Ion kinetic dampening is accelerated because of a higher gas pressure in the beginning of the ion guide 83. The local raise of gas pressure is formed by gas confining cap 74C and by a gas jet, emerging of the aperture 74.

Trapped ions get confined in the DC potential well, formed with the aid of additional electrodes 84. Such electrodes surround RF rods 83 of the second ion guide 81, such that to make an effective and symmetric penetration of potentials of the additional electrodes. Referring to the electrostatic field on the axis of the ion guide 81, a set of additional electrodes 84 forms an axial distribution of DC field while generating a moderate octupole DC field in the radial direction. It is important to keep such octupole DC field small enough to avoid ion instability during a long term storage. As a numeric example, an RF potential of 1.5kV and 3Mhz frequency is applied to 5mm quadrupole rods positioned on 10mm diameter between centers. Each additional electrode is formed as a plate having central hole of 5mm and 7mm holes for rods. About 20% of potential of such plate penetrates to the center of quadrupole assembly. Three plates are located 3mm apart from each other and 5mm away from the exit aperture. By applying 10V drop to the central plate we form a DC well of c.a. 2V deep. Ions with energy of 100meV are confined into cloud of c.a. 1mm long and fraction of mm in diameter. The arrangement has very little effect on ion stability and allows storing of ions within at least one decade of mass to charge ratio.

After collisional dampening and confinement in the ion guide 81 the ion packet get axially ejected (in the X direction) into the DC accelerator 92 and then into the MR TOF analyzer 31. After emptying of second storage the pulsed potentials are returned to their trapping state to prepare for the next cycle of ion storage. The pulsed ejection is made with the aid of high voltage electric pulses, applied to the set 84 of additional electrodes and to the exit aperture 88, while keeping RF potentials unchanged. Low gas pressure in the second storing quadrupole 81 helps avoiding gas discharges while applying high voltage pulses. Since all the ions are stored in the small area such pulses do not spill any other ions and pulse amplitude could be fairly high - enough to noticeably reduce ion turn around time. Thus, ability of compressing ion packet into a small cloud and ability of applying high voltage accelerating pulses are, in fact, another two important reasons for dual storage arrangement. Such ion packet parameters could not be achieved in case of fast ejecting directly out first ion guide 71.

Application of fairly large ejecting pulses causes a substantial reduction of ion turn around time and thus allows using an ion guide as a direct pulsed ion source for MR TOF MS. In our ion optics simulations, made for the above geometrical example, we found that by applying high voltage pulses to the additional electrodes the turn around time could be reduced to few nanoseconds. For example, by applying 5kV pulse to the middle additional electrode (out of three) and –1kV pulse to exit aperture, an axial field reaches c.a. 200V/mm. Assuming 200meV initial energy spread and 1mm size of stored ion cloud, the turn around time of 1000amu ions is 10ns only and the energy spread of ejected ion packets is below 200eV. By applying a c.a. 4kV DC post - acceleration in the DC accelerator 92 the ion beam has less than 5% energy spread, is well focused and has a phase space below 10π*mm*mrad, which is well compatible with the wide acceptance and high order time-of-flight focusing of the MR TOF analyzer of the invention.

In ion optics simulations by inventors the resolution of the MR TOF MS appears to be mostly limited by turn around time. As a numerical example, ions of 1000amu, accelerated to 4keV energy and Velocity 3×10^4 m/s have 10ns turn around time, while having 1ms flight time in 1m analyzer with 12 reflections. Such analyzer provides a folded path with the effective flight path of 30m. If 10ns turn around time is indeed the only limiting factor, then resolution reaches R=50,000. Further extension of flight time is expected to improve resolution even more. A longer

accumulation would cause some deterioration of the turn around time. However, the raise of space charge field and of the turn around time is expected to be slower than the raise of flight time.

The scheme allows 100% conversion of continuous ion beam into ion packets. Besides, achievable parameters of ion packets allow a complete transmission of ions through the novel MR TOF MS and if turn around time is the major limiting factor then it still allows reaching a 50,000 resolution within a 1m long instrument, employing 12 full turns. Those parameters exceed resolution and sensitivity of existing o-TOF MS as well as superior to the existing MR TOF MS by sensitivity.

The described preferred embodiment is meant to be an explanatory example, not intended to be limiting. Further, it may be apparent to those skillful of the art, that numerous changes could be made while staying within the spirit and principle of the invention.

CLAIMS

What is claimed is:

1. A multi reflecting time-of-flight mass spectrometer (MR TOF MS) comprising:
A pulsed ion source;
An ion receiver;
A set of two parallel gridless ion mirrors, substantially elongated in one – 'shift' direction;
A field-free drift space between the said mirrors;
The above elements being arranged to provide a folded ion path between the ion source and the receiver, composed of multiple reflections between the ion mirrors and of a drift in the shift direction;
The said MR TOF MS separating ions in time according to their mass to charge ratio such that the flight time is substantially independent of ion energy;
wherein for the purposes of improving resolution and sensitivity a set of 2 or more lenses is positioned in the said drift space along said shift direction, with a period corresponding to ion shift per integer number of ion reflections.
2. The MR TOF MS of claim 1, wherein each of the said ion mirrors comprises at least 4 electrodes to provide independence of time-of-flight focusing of ions on initial spatial spread across the plane of the folded ion path.
3. The MR TOF MS of claim 1 **or 2**, wherein the said pulsed ion source comprises an ion storage device, a pulsed ion accelerator whereas ions are produced by an intrinsically continuous ion source of the following list: ESI, APCI, EI, CI, PI, ICP, gas filled MALDI, or a fragmentation cell of a tandem mass spectrometer.
4. The MR TOF MS of claim 1 **or 2**, wherein ions in the said pulsed ion source are produced by a pulse of either ions or electrons or photons and wherein said source preferably incorporates any of the following devices: a) a pulsed gas supply b) an accelerator with pulsed voltages c) an accelerator with static voltages.
5. The MR TOF MS of claim 3, wherein the said ion storage device is a gas-filled set of electrodes with radio-frequency voltage applied to at least one of them including any device of the following list: ion guide, ion trap, linear ion trap, RF channel.
6. The MR TOF MS of claim 3, wherein the said pulsed ion accelerator is an orthogonal accelerator for accelerating ions in the direction orthogonal to the shift direction, preferably elongated and oriented along the shift axis of the MR TOF MS.
7. The MR TOF MS of claim 3 **or 4 or 6**, wherein the said accelerator is built into the pulsed ion mirror, or positioned adjacent to the ion mirror and has matching electrode shape and potentials.
8. The MR TOF MS of claim 3 **or 5**, wherein the said continuous ion source comprises an additional storage ion guide, preferably having a higher gas pressure compared to the ion storage device of claim 3 and wherein said additional storage ion guide is a gas-filled set of electrodes with radio-frequency voltage applied to at least one of them including any device of the following list: ion guide, ion trap, linear ion trap, RF channel.
9. The MR TOF MS of claim 8, wherein the said ion storing device contains two sets of elongated electrodes, with radio-frequency voltages applied to electrodes of the first set and pulsed voltages applied to at least one electrode of the second set.
10. The MR TOF MS of claim 1, wherein for the purpose of convenient tuning the periodic lenses are substantially elongated transversely the plane of the folded ion path

11. The MR TOF MS of claim 1, wherein the said elongated ion mirrors are made as a parallel assembly of conductive square frames, plates with long slots, bars, rods or a like with an optional edge termination by printed circuit boards.
12. The MR TOF MS of claim 2, wherein each of the said mirrors comprises at least two electrodes having voltages of opposite polarities relatively to each other.
13. The MR TOF MS of claim 1, wherein at least one electrode of at least one ion mirror is connected to a pulsed voltage supply for ion gating in and/or out of the MR TOF MS.
14. The MR TOF MS of claim 1, wherein the drift space comprises means for ion deflection, connected to either a DC or pulsed voltage supplies.
15. The MR TOF MS of claim 14, wherein the said deflection means comprises at least one set of steering plates, either planar or bent.
16. The MR TOF MS of claim 15, wherein the ion receiver is located approximately on the line of sight with the ion accelerator on the entrance side of the shift axis, wherein one set of steering plates is located on the far side of the shift axis and wherein another set of steering plates on the entrance side allows switching between two modes: a) ion deflection into a folded ion path through both ion mirrors and the first set of steering plates; b) bypassing of MR TOF MS and diverting ion beam directly into the ion receiver.
17. The MR TOF MS of claim 15, wherein at least one set of steering plates is located between pulsed ion source and the first ion mirror along said folded ion path, and at least one set of steering plates is located between the last ion mirror along said folded ion path and ion receiver, those sets being connected to a pulsed voltage supplies to control a number of ion reflections within the said folded ion path.
18. The MR TOF MS of claim 15, wherein the steering plates have the same dimensions as electrodes of the planar lenses of claim 13 and wherein at least one steering plate is adjusted to either combine focusing and steering or to be switched between those.
19. The MR TOF MS as claimed in any one of claims 1 to 4, wherein the ion receiver is a fragmenting cell, combined with an additional time-of-flight mass spectrometer for mass analysis of fragment ions.
20. The MR TOF MS as claimed in any one of claims 1 to 4, wherein the ion receiver is an ion detector, connected to a transient recorder, both preferably having an extended dynamic range.
21. A method of sample analysis using multi reflecting time-of-flight mass spectrometer, said method comprising the sequential steps of:

Forming ions packet in a pulsed ion source;

Passing ions along a multiply folded ion path, formed by reflecting ions within a two-dimensional electrostatic field and by ion drift in a third - 'shift' direction;

Receiving ions, time separated according to their mass to charge ratio onto an ion receiver;

The said electrostatic field being formed within two planar and parallel gridless ion mirrors, surrounding a field–free space;

The said ion mirrors being tuned to simultaneously achieve a time-of-flight focusing and a spatial focusing across the plain of the folded ion path;

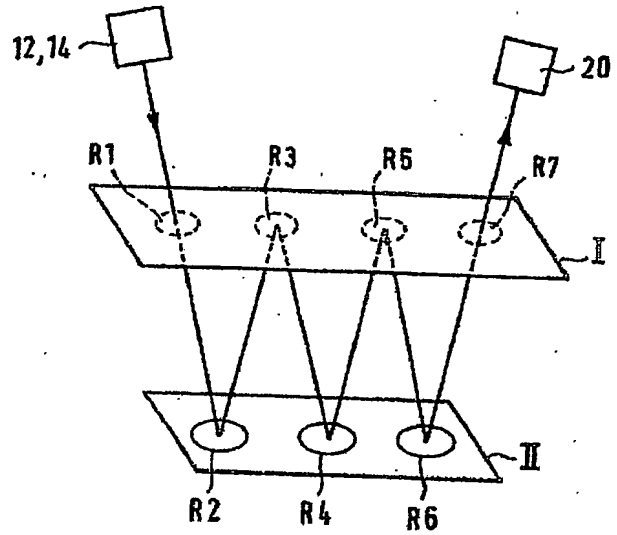
wherein for the purposes of improving resolution, sensitivity and ease of use, the ion packets are periodically focused in the shift direction by a set of multiple periodic lenses;

and wherein the said ion mirrors are arranged and tuned to provide a time of-flight focusing, substantially independent on ion width across the plane of ion path.

22. The method of claim 21, wherein the said ion packets are produced by an ionization method of the following list: SIMS, MALDI, IR MALDI, preferably incorporating a pulsed gas cooling, and wherein the said pulsed acceleration is delayed compared to the ionizing and cooling pulses.
23. The method of claims 21, wherein the said ion packets are produced in the following sequence of steps: a continuous ion beam is produced by a continuous ionization method, like ESI, APCI, EI, CI, PI, ICP, SIMS or MALDI with collisional cooling; the said continuous ion beam is stored in a gas-filled volume using ion confinement by a combination of RF and DC electric fields with a subsequent pulse ejection and acceleration of ion packets.
24. The method of claim 23, wherein the said pulsed acceleration is made by pulsed change of said DC fields within gas-filled volume without substantially changing RF field.
25. The method of claim 23, wherein the said pulsed ejection is composed of two separate, frequency synchronized and time delayed steps- ejection from the gas-filled volume and a subsequent orthogonal pulsed acceleration in the orthogonal direction.
26. The method of claim 23, wherein the said continuous ion source comprises an additional step of ion storage and partial ejection of stored ion cloud, the said step being performed at a higher gas pressure, compared to the storage step preceding acceleration of ion packets.
27. The method of claim 21, wherein the said time focusing is achieved to a second order in relation to spatial, angular and energy spreads of the initial ion packet , including cross terms and wherein possible temperature and time distortions of such focusing are compensated by adjusting a single potential of ion mirror electrodes, preferably of the end electrodes.
28. The method of claim 21, wherein the said set of periodic lens is adjusted to make focal length F approximately equal to an integer number of quarter turns, F=N*P/4, where N=1,2,3...
29. The method of claim 21, wherein the said ion spatial and time-of-flight focusing by the said ion mirrors is achieved using mirrors with 4 to 7 electrodes while the spatial focusing transversely the plane of the folded ion path is achieved by incorporating a lens into the planar ion mirror, such lens having potential of opposite polarity relatively to field-free space.
30. The method of claim 21, wherein said ion mirrors are formed by fewer than 4 electrodes with a curved two-dimensional shape of electrodes.
31. The method of claim 21, wherein at least one electrode of at least one ion mirror is pulsed for ion gating in and/or out of the MR TOF MS, initial acceleration, selection of number of cycles or discarding of ions outside of the desired mass range.
32. The method of claim 21, wherein for the purpose of convenient tuning the periodic lens is substantially elongated across the shift axis.
33. The method of claim 21, wherein ions are reflected along the shift direction, using a constant and/or a pulsed operated reflection to form a folded path with or without repetitive segments, to gate ions in and out of the MR TOF MS, to bypass the MR TOF MS and to control number of repetition cycles.
34. The method of claim 21, wherein deflection plates are arranged within field-free space to provide mutual compensation of chromatic aberrations occurring in ion mirrors, lens and deflection plates.
35. The method of time-of-flight mass analysis, wherein the method of claim 21 is a part of a multiple-stage mass-spectrometric analysis or separation.

ABSTRACT

The present invention relates generally to the area of mass-spectroscopic analysis, and more in particularly is concerned with the apparatus, including a multi reflecting time-of-flight mass spectrometer (MR TOF MS). In this spectrometer the flight path of ions from an ion source to a receiver is folded along a jig-saw trajectory by two parallel gridless electrostatic mirrors, substantially elongated in the shift direction, orthogonal to the direction of reflection. For the purposes of improving sensitivity a set of multiple lenses is positioned in the drift space between the mirrors to provide for spatial focusing of ions in the plane of the folded ion path. Besides, for improving both sensitivity and resolution each mirror consists of at least 4 electrodes arranged and controlled so that to improve ion optics properties. Namely, in addition to time-of-flight focusing in energy and spatial focusing across the plane of the folded ion path, the mirrors also provide time-of-flight focusing with respect to the spatial spread of ions across the said plane. Because of improved spatial and time focusing, the MR TOF MS of the invention provides for a wider acceptance and confinement of ion beam along an extended folded ion path. As a result, the MR TOF MS of the invention can be efficiently coupled to continuous ion sources via an ion storing device, thus improving efficiency of ion sampling.



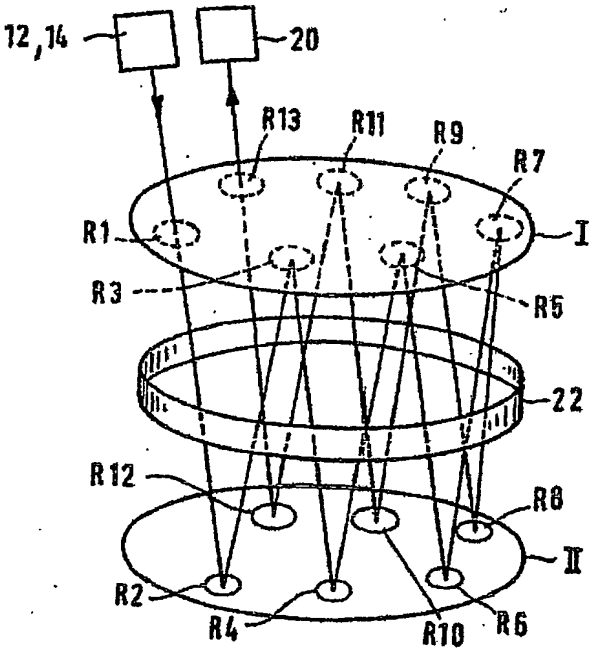


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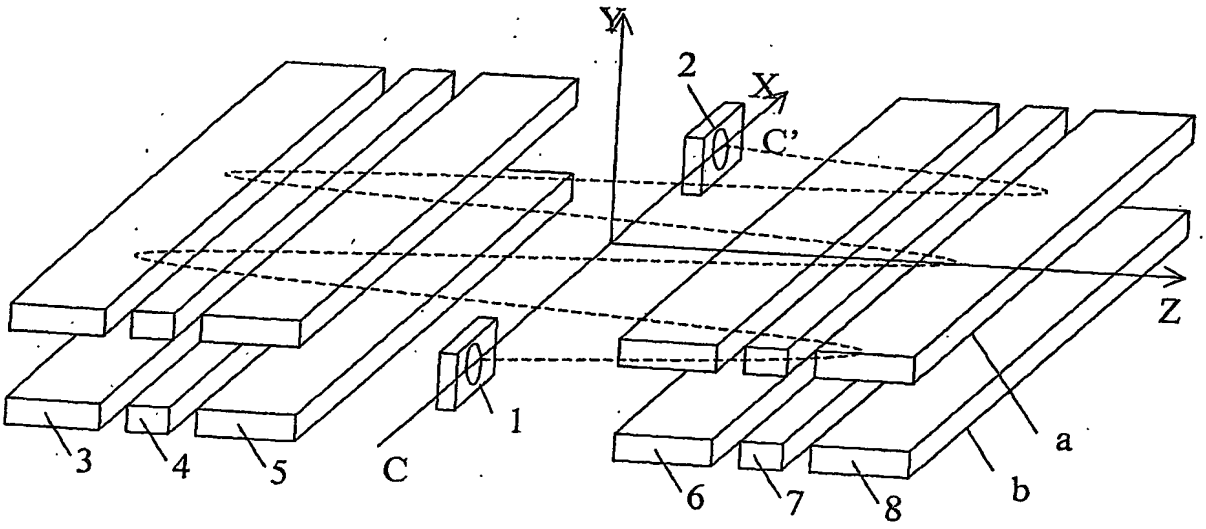
Fig.1



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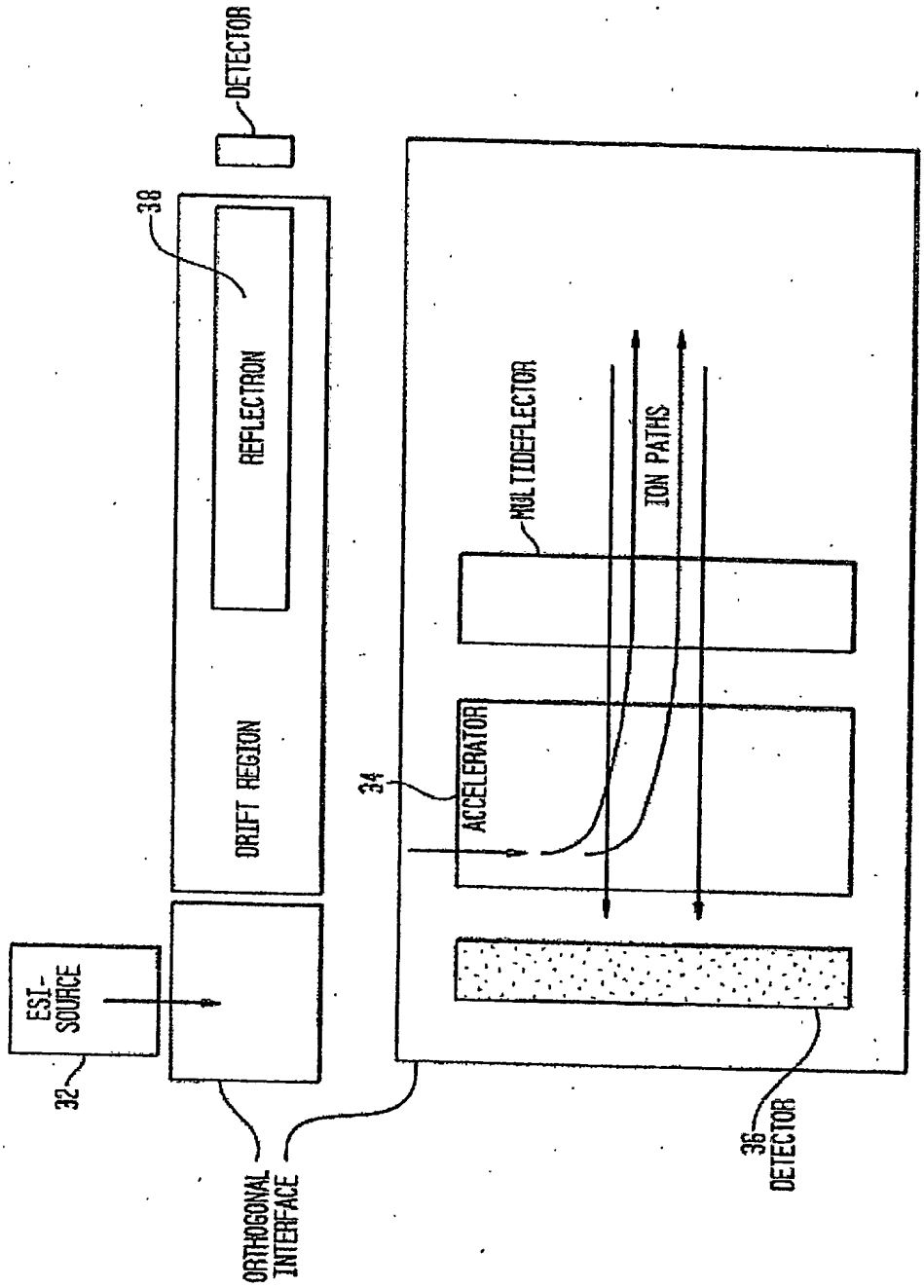
Nazarenko et.al. SU 1725289

Fig.2



PRIOR ART, M. Park, US6107625

Fig.3

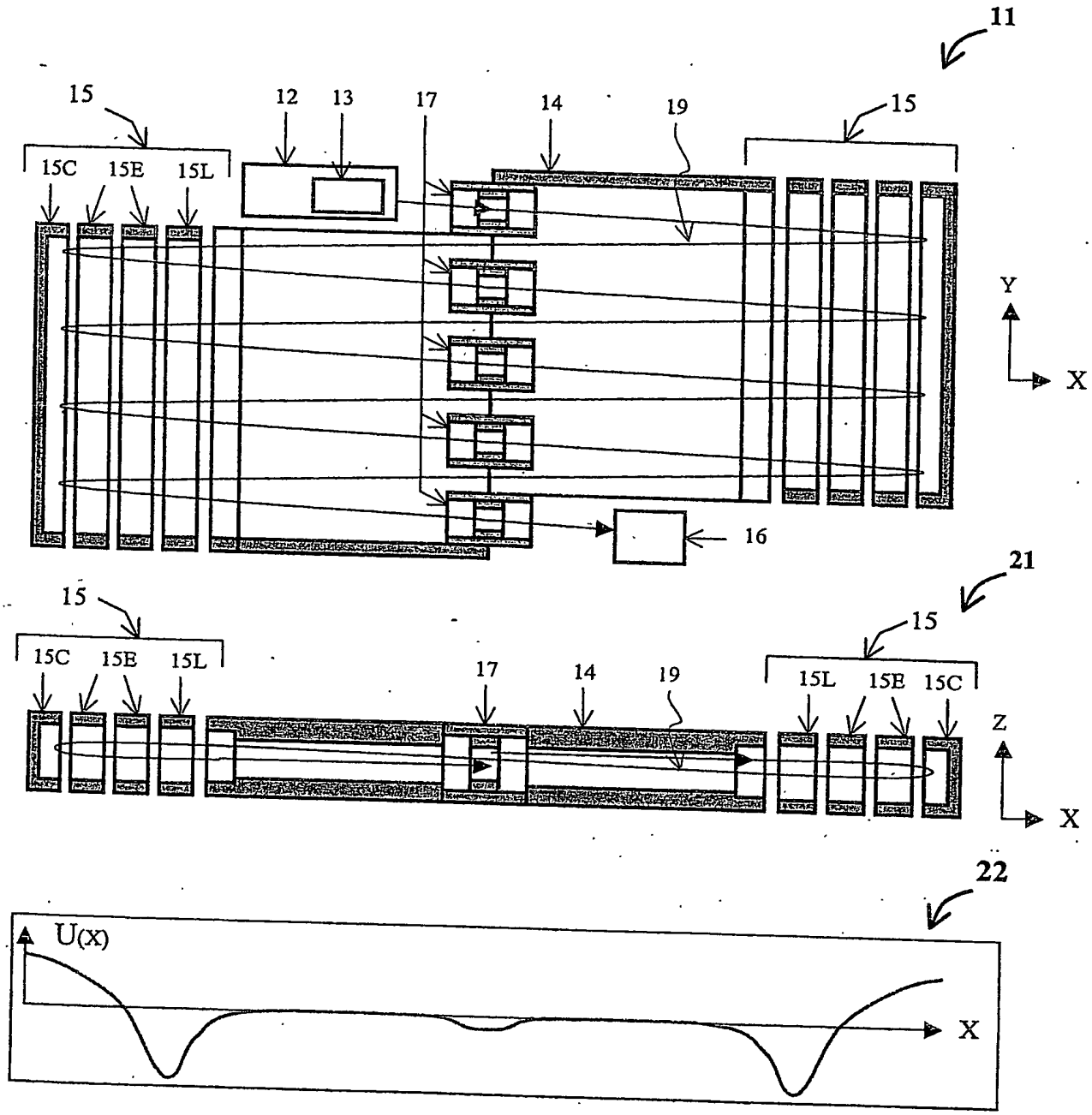

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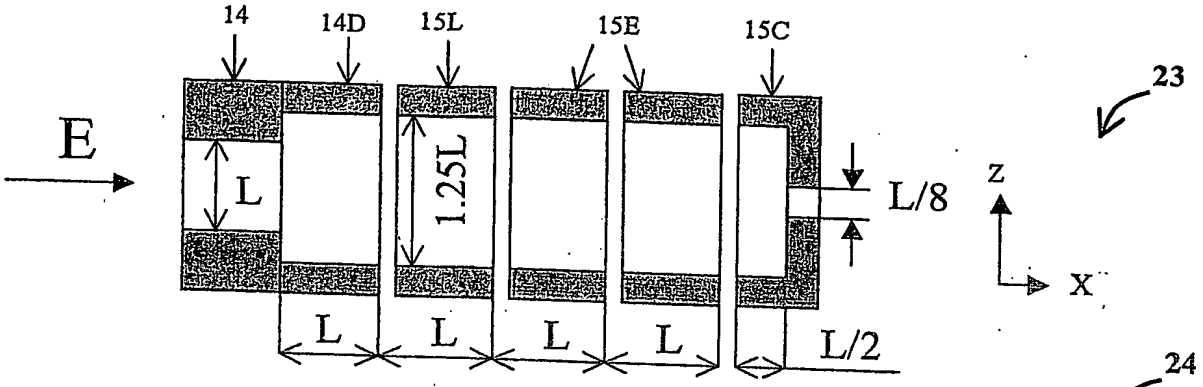
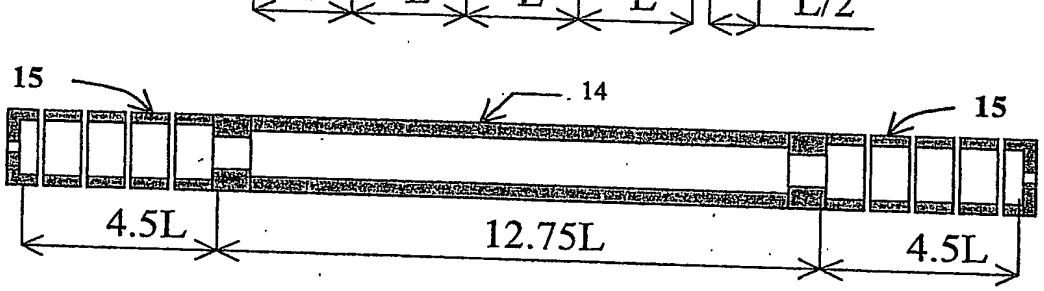
Fig.4





Electrode	14 Drift	15L Lens	15E electr 1	15E electr 2	15C Cap
U/E	0	-2.0842	.1766	0.9616	1.3148

25

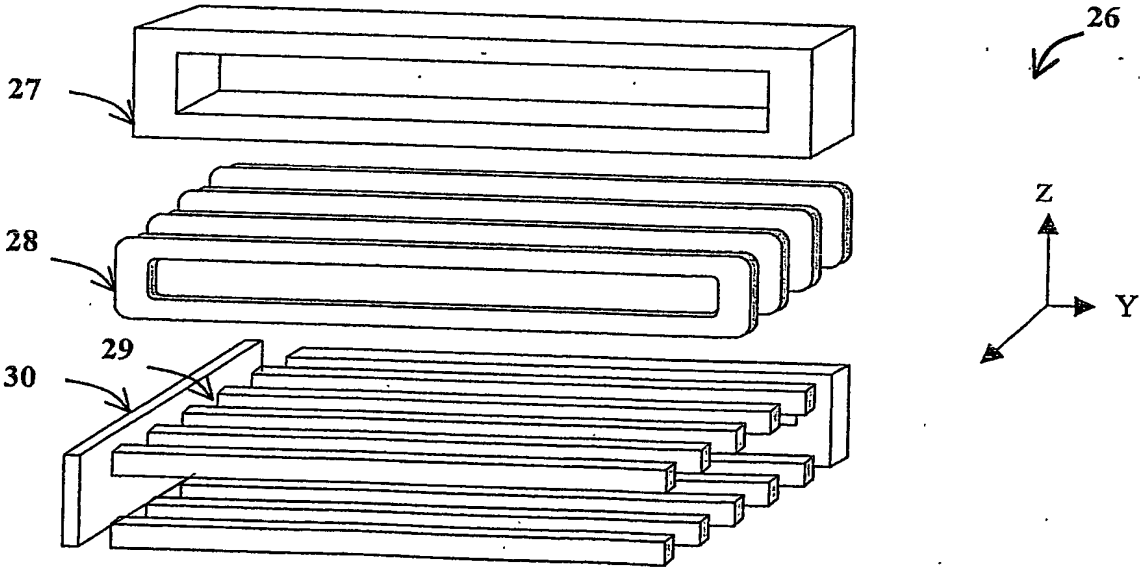
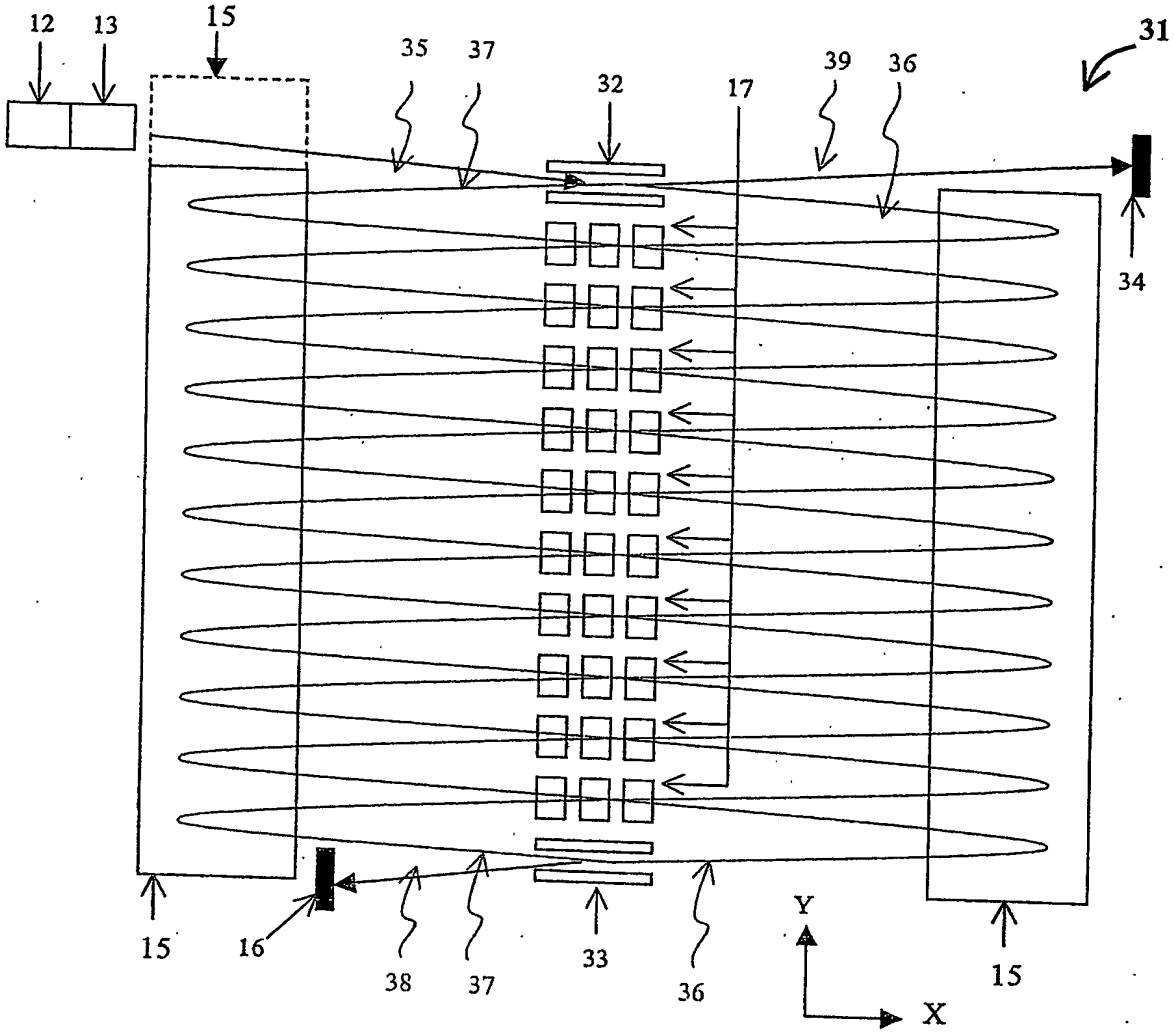


Fig.5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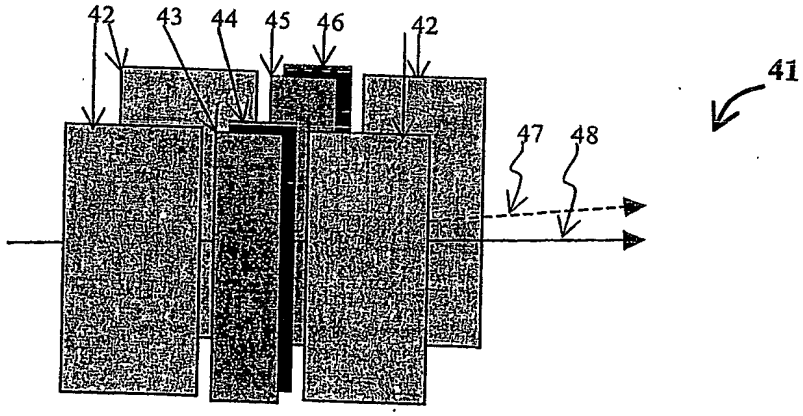
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Fig.6

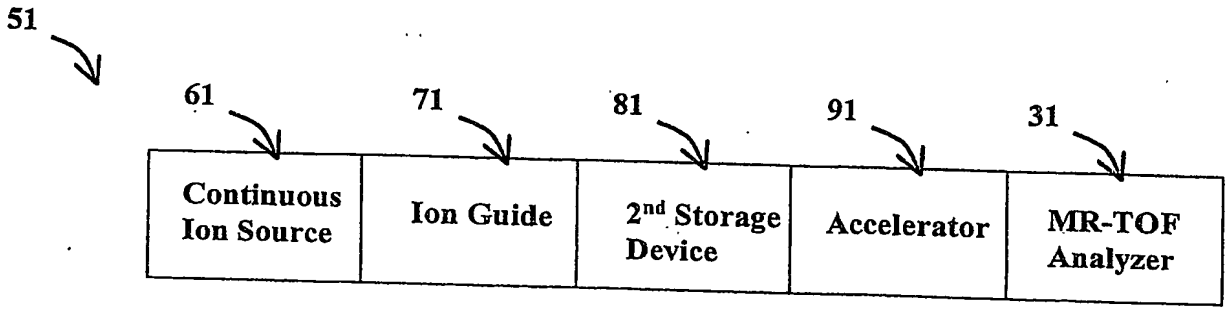

Fig. 7A

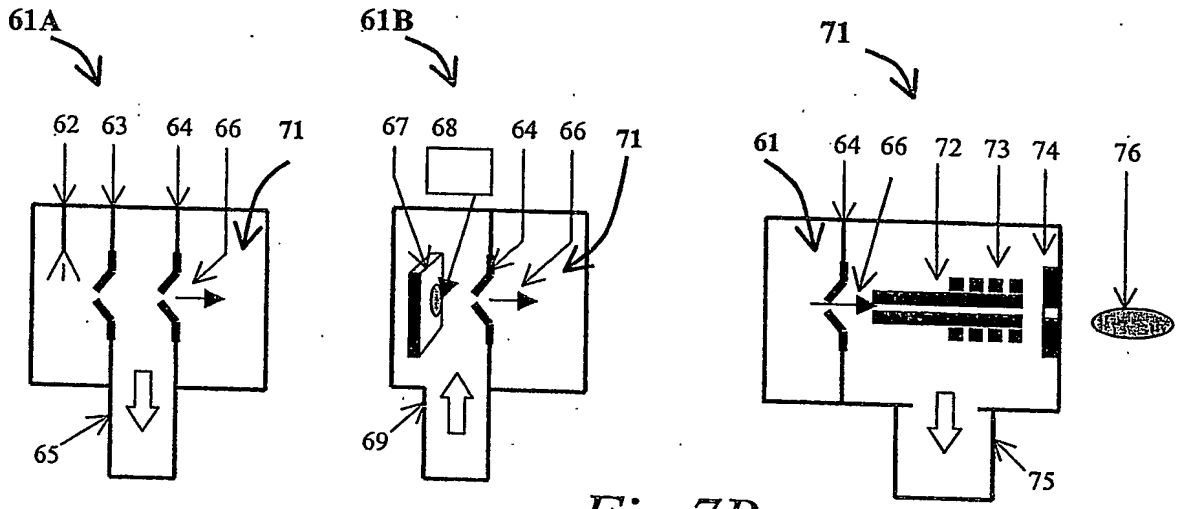

Fig. 7B

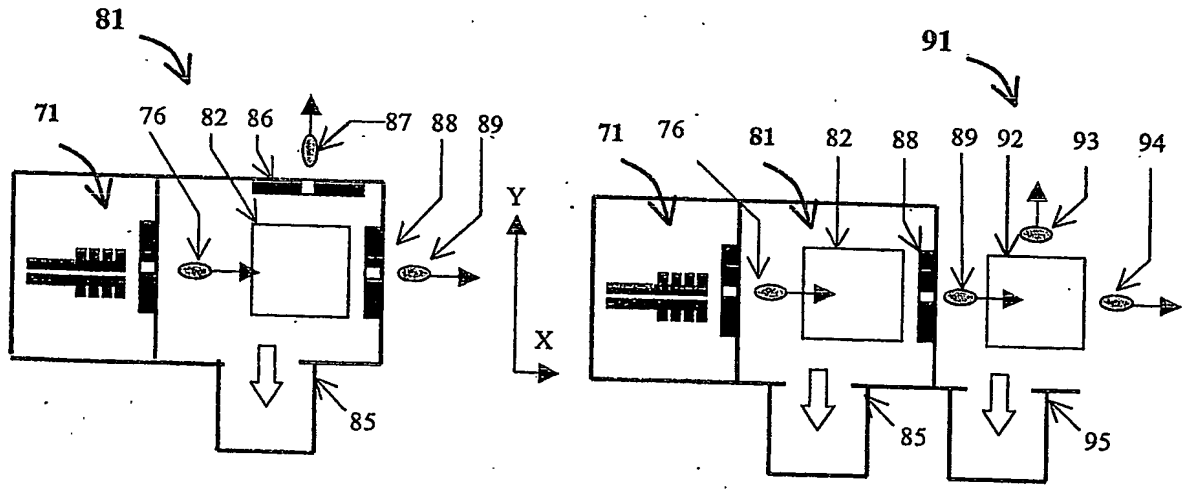

Fig. 7C

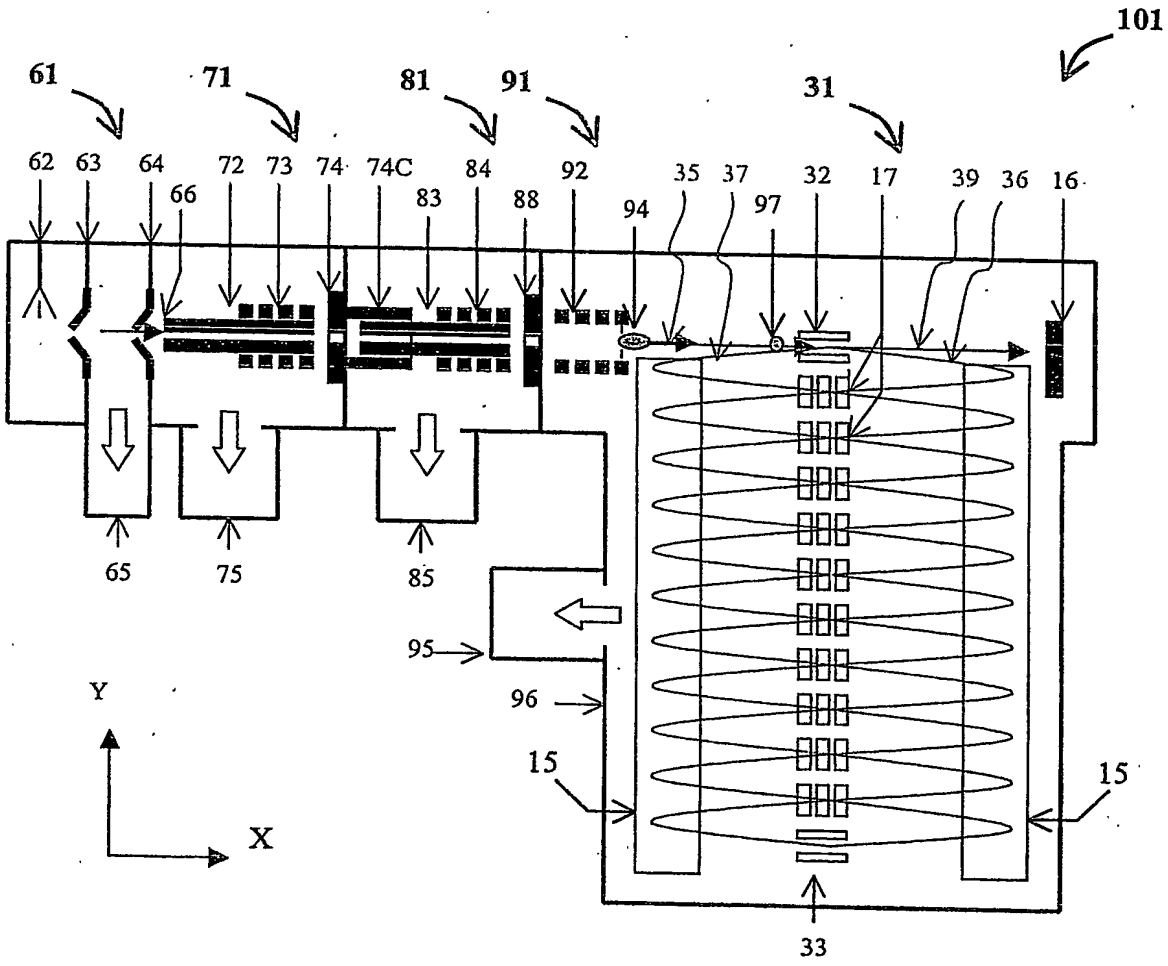
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Fig.8

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